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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/570,909	03/29/2006	Carsten Hopf	14129-00001-US	1220

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EXAMINER	
HILL, KEVIN KAI	

ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/570,909	HOPF, CARSTEN	
	Examiner	Art Unit	
	Kevin K. Hill, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Amendments

In the reply filed July 9, 2007, Applicant has cancelled Claims 1-6 and 12-68 and amended Claims 7 and 10-11. Claims 7-11 are under consideration.

Priority

1. This application is a 371 of PCT/EP04/09771, filed September 2, 2004. Acknowledgment is made of Applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). Certified copies of the following foreign applications have been provided:

EPO 03019642.2, filed September 5, 2003,
PCT/EP2003/013980, filed December 10, 2003,
EPO 04001895.4, filed January 29, 2004,
EPO 04001894.7, filed January 29, 2004,
EPO 04007447.8, filed March 26, 2004,
PCT/EP2004/004891, filed May 7, 2004,
PCT/EP2004/004889, filed May 7, 2004, and
EPO 04018874.0, filed August 9, 2004.

Response to Amendment

Applicant has provided to the Examiner locations in EPO 03019642.2, filed September 5, 2003, that support the instant invention. Accordingly, the effective priority date of the instant application is granted as September 5, 2003.

Examiner's Note

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment will not be reiterated. The arguments in the July 9, 2007 response will be addressed to the extent that they apply to current rejection(s).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. **Claims 7-11 stand rejected under 35 U.S.C. 103(a)** as being unpatentable over Winther et al (WO 01/70993 A2, September 27, 2001) and Fechteler et al (WO 01/49871 A2, July 12, 2001).

The claims are drawn to a method for identifying a gamma secretase modulator, comprising the steps of identifying a FADS2-interacting molecule, wherein the FADS2-interacting molecule binds to, and inhibits FADS2, and determining whether the FADS2-interacting molecule is capable of modulating gamma secretase, as measured by the ability of amyloid precursor protein (APP) to be cleaved.

Winther et al teach a method for identifying a compound that inhibits the activity of delta-6-desaturase (also known in the art as FADS2, see pg 4, line 1 of the instant specification) (pg 3, [0028]). Winther et al teach that host systems in which the method(s) may be performed include *in vivo* and *in vitro* systems (pgs 14-15, [0166-1076]). Winther et al contemplate that potential agonists include small molecules that bind to FADS2 polypeptides, and thereby extinguish its activity, by prevent binding to cellular binding molecules, e.g. regions of FADS2 which contact other proteins and/or localize the FADS2 within a cell, and regions which bind substrate, such that normal activity is prevented (pgs 17-18, [0201-0204]). Winther et al teach a composition for the treatment of a lipid metabolism disorder, comprising a compound identified by the inventive method and a pharmaceutically acceptable carrier (pg 3, [0031]), wherein contemplated disorders include neurodegenerative diseases such as Alzheimer's disease and diabetic neuropathy (pg 4, [0037]).

Winther et al do not teach the method step of determining whether the FADS2-interacting molecule is capable of modulating gamma secretase activity, as recited in Claims 7 and 10. However, at the time of the invention, Fechteler et al taught methods of finding inhibitors of membrane-based proteases, in particular gamma secretase (pg 1, [0002]; pg 4, [0062]). The compounds identified by the inventive method(s) are contemplated to be useful for the treatment of neurodegenerative disorders, e.g. Alzheimer's disease, Parkinson's disease and Huntington's chorea (pg 4, [0065]). Fechteler et al taught that the activity of gamma-secretase may be measured by the ability of gamma-secretase to cleave a reporter protein that comprises a fragment of amyloid β, specifically the C99 fragment (pg 3, [0040-0044]), or endogenous Aβ polypeptides (pg 8, [0113-0114], Example 8).

It would have been obvious to one of ordinary skill in the art to modify the method of Winther et al as taught by Fechteler et al with a reasonable chance of success because Fechteler et al teaches methods of assaying for APP cleavage. An artisan would be motivated to make such modifications because gamma secretase is a holoenzyme comprising Presenilin, Nicastrin and Pen2 subunits, each of which are associated with FADS2, and thus a FADS2-interacting molecule that interferes with FADS2 activity or binding to cellular proteins would likely affect the formation of the gamma-secretase holoenzyme, as measured by gamma-secretase activity taught by Fechteler et al.

Thus, the invention as a whole is *prima facie* obvious.

Applicant's Arguments

Applicant argues that Winther et al do not teach or suggest the identified molecules could modulate gamma secretase activity, or that gamma secretase modulation of such molecules should be determined. Fechteler et al. do not teach or suggest that these gamma secretase inhibitors could be FADS2 interacting molecules. At the time the present application was filed, it was known in the art that molecules beneficial in treating Alzheimer's disease might have completely diverse mode of action and involve various pathways or mechanisms in the cell. Absent the hindsight afforded by a reading of Applicant's disclosure, a person of ordinary skill, upon reading Winther et al. and Fechteler et al., would not have motivation to test whether the molecules identified in Winther et al. might also modulate gamma secretase activity.

Applicant's argument(s) has been fully considered, but is not persuasive.

In response to Applicant's argument that the references do not provide that a specific teaching, suggestion, or motivation to support a finding of obviousness, *KSR* forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. See the recent Board decision *Ex parte Smith*, USPQ2d, slip op. at 20 (Bd. Pat. App. & Interf. June 25, 2007) (citing *KSR International Co. v. Teleflex Inc. (KSR)*, 82 USPQ2sd at 1396) (available at www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf).

In response to Applicant's argument that the Examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the Applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Applicant's argument that molecules beneficial in treating Alzheimer's disease might have completely diverse mode of action and involve various pathways or mechanisms in the cell, as per the teachings of Doraiswamy (CNS Drugs 16(12): 8211-824, 2002) has been considered.

However, at the time of the invention, the general knowledge in the art recognized that gamma secretase is a holoenzyme comprising Presenilin, Nicastrin and Pen2 subunits, each of

which are associated with FADS2. Thus, it would have been well within the ordinary ingenuity of the artisan and obvious to try testing whether or not a newly identified FADS2 inhibitor that interferes with FADS2 activity or binding to cellular proteins as taught by Winther et al would also inhibit gamma secretase because of the art-recognized interaction between FADS2 and multiple members of the gamma secretase holoenzyme, a FADS2-interacting molecule that interferes with FADS2 activity or binding to cellular proteins would likely affect the formation of the gamma-secretase holoenzyme, and means of measuring gamma-secretase activity were of general knowledge in the art.

Conclusion

3. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Kevin K. Hill, Ph.D. whose telephone number is 571-272-8036. The Examiner can normally be reached on Monday through Friday, between 9:00am-6:00pm EST.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Joseph T. Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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